

Listing of claims

1 - 20 (canceled)

21. (previously presented) A protein having a formula selected from the group consisting of R_1 - R_2 and R_1 -L- R_2 , wherein R_1 is a Fc protein, or a variant or fragment thereof, R_2 is a variant or fragment of an osteoprotegerin (OPG) protein selected from a deletion of one or more amino acids from positions 186-401 as shown in Figure 2 (SEQ ID NO:2) or a truncation of an amino acid sequence from positions 22-X as shown in Figure 2 (SEQ ID NO:2) wherein X is any residue from position 185 to 293 inclusive, and L is a linker, wherein the protein has the activity of decreasing bone resorption.

22. (previously presented) The protein according to claim 21, wherein the Fc protein is selected from one or more of:

(a) the Fc amino acid sequences as set forth in Figure 1 (SEQ ID NO:1);

(b) the amino acid sequence of subpart (a) having a different amino acid substituted or deleted in one or more of the following positions (using the numbering according to Figure 1 (SEQ ID NO:1)):

(i) one or more cysteine residues;

(ii) one or more tyrosine residues;

(iii) cysteine at position 5 deleted or substituted with an alanine;

(iv) leucine at position 20 deleted or substituted with glutamine;

(v) glutamic acid at position 103 deleted or substituted with an alanine;

(vi) lysine at position 105 deleted or substituted with an alanine;

(vii) lysine at position 107 deleted or substituted with an alanine;

(viii) deletion or substitution of one or more of the amino acids at positions 1, 2, 3, 4, and 5;

(ix) one or more residues substituted or deleted to ablate the Fc receptor binding site;

(x) one or more residues substituted or deleted to ablate the complement (C1q) binding site; and

(xi) a combination of subparts i-x;

(c) the amino acid sequence of subparts (a) or (b) having a methionyl residue at the N-terminus;

(d) the Fc protein, or variant, fragment or derivative thereof, of any of subparts (a) through (c) comprised of a chemical moiety connected to the protein moiety;

(e) a derivative of subpart (d) wherein said chemical moiety is a water soluble polymer moiety;

(f) a derivative of subpart (e) wherein said water soluble polymer moiety is polyethylene glycol; and

(g) a derivative of subpart (e) wherein said water soluble polymer moiety is attached at solely the N-terminus of said protein moiety.

23. (previously presented) The protein according to claim 21 further comprising a methionyl residue at the N-terminus.

24. (previously presented) The protein of claim 21 wherein the linker comprises one or more amino acids selected from any one or more of glycine, asparagine, serine, threonine and alanine.

25. (previously presented) The protein of claim 21 wherein the linker is selected from:

(a) ala-ala-ala;

(b) ala-ala-ala-ala (SEQ ID NO: 51);

(c) ala-ala-ala-ala-ala (SEQ ID NO: 52);

(d) gly-gly;

(e) gly-gly-gly;

- (f) gly-gly-gly-gly-gly (SEQ ID NO: 53);
- (g) gly-gly-gly-gly-gly-gly-gly (SEQ ID NO: 54);
- (h) gly-pro-gly;
- (i) gly-gly-pro-gly-gly (SEQ ID NO: 56);
- (j) val;
- (k) ser-gly-gly-gly-gly-gly-gly-gly-gly (SEQ ID NO: 56);
- (l) gly-gly-ser-gly-ser-ala-gly-ser-gly-ser-gly-gly-ser-gly-ser-gly-gly (SEQ ID NO: 57);
- (m) a chemical moiety; and
- (n) any combination of subparts (a) through (m).

26. (previously presented) A fusion protein comprising an amino acid sequence selected from the amino acid sequences set forth in Figures 5, 6, 7 or 8 (SEQ ID NOS: 5, 6, 7, 8, respectively).

27. (previously presented) The protein of Claim 21 comprising a chemical moiety covalently attached to the protein.

28. (previously presented) The protein of Claim 27 wherein the chemical moiety is a water soluble polymer.

29. (previously presented) The protein of Claim 28 wherein the water soluble polymer is selected from one or more of polyethylene glycol and polyamino acid.

30. (previously presented) The protein of Claim 29 wherein the water soluble polymer moiety is attached solely at the N-terminus of the protein.

31. (previously presented) A pharmaceutical composition comprising a protein according to any of Claims 21 to 26 in an amount effective to decrease bone resorption in a pharmaceutically acceptable diluent, adjuvant and/or carrier.